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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,587	02/21/2006	William E. Beschoner	000241.00003	1006

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EXAMINER

SAJJADI, FEREDYDOUN GHOTB

ART UNIT	PAPER NUMBER
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1633

MAIL DATE	DELIVERY MODE
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10/17/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/527,587	Applicant(s) BESCHORNER ET AL.	
	Examiner FEREYDOUN G. SAJJADI	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 4 and 6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5 and 7-22 is/are rejected.
- 7) ☒ Claim(s) 5 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/7/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission and amendment filed on August 1, 2008, that includes a response to the office action dated April 1, 2008, has been entered. Claims 1-4 have been amended, and claims 13-22 newly added. No claims were cancelled. Accordingly, claims 1-22 are pending in the application. Claim 6 remains withdrawn from consideration, without traverse. Claim 4 is newly withdrawn, as drawn to non-elected species of the invention. The elected species of tissue is liver, now cancelled from claim 4.

Claims 1-3, 5 and 7-22 are currently under examination. The claims have been examined commensurate with the elected invention and the species of invention.

New Claim Objections

Claim 5 is newly objected to because of the following informalities: The claim recites "an artiodactyls", that should be in the singular form. Appropriate correction is required.

Applicant is advised that should claim 17 be found allowable, claim 19 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Response & New Claim Rejections - 35 USC § 102

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Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 1, 2, 4, 5, 7 and 8 stand rejected under 35 U.S.C. §102(e) as being anticipated by Wu et al. (U.S. Patent No.: 6,995,299; filed Aug. 15, 2001). The rejection set forth on pp. 3-4 of the office action dated August 20, 2007, and pp. 2-3 of the previous office action dated April 1, 2008 is maintained for claims 1, 2, 5, 7 and 8, and further applied to new claims 13-21 for reasons of record.

Applicants traverse the rejection, arguing that Wu explicitly teaches that prenatal destruction of hepatocytes before colonization with human hepatocytes should be avoided; Wu teaches that one should not use a transgene to "selectively destroy[ing] native cells in a tissue of a fetal non-human mammal host,"; Wu also teaches reduction of host liver cells by administering a drug which liver cells metabolize to a toxic agent; Applicants concluding that the teachings do not anticipate claim 1, which explicitly recites "destroying native cells in a tissue of a fetal non-human mammal host". Applicants' arguments have been fully considered, but are not found persuasive.

In response, it is noted that Applicants have based their arguments on selected teachings of Wu et al., and interpreting the select teachings out of context, thus leading to a faulty conclusion. Wu teaches a number of different embodiments of their invention. As previously indicated, Wu et al. state: "selection pressure may be used to favor the proliferation of human hepatocytes. Such selection pressure is defined herein as including any condition, preexisting in the host animal at the time of introduction of donor cells or imposed thereafter, which results in a greater likelihood that human hepatocytes, rather than host hepatocytes, will proliferate. For example, the selection pressure may result from the presence of a transgene that decreases the viability of host hepatocytes, either intrinsically (directly) or by administration of an activating agent (indirectly)... the transgene may be the albumin promoter/HSV-TK construct, whereby when gancyclovir is administered to the host animal (e.g., as an intraperitoneal injection of 250 mg/kg gancyclovir in sterile PBS), hepatocytes of the transgenic host may be selectively killed. In such embodiments, the death of host hepatocytes would be expected to favor compensatory proliferation of human hepatocytes." (column 18, lines 20-48). Thus, the human foreign replacement cells replace destroyed cells of the liver tissue.

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Wu et al. teach that the animal comprising human hepatocytes is preferably a fetus (col. 5, line 5), and state: "To avoid destroying the animal's liver prior to colonization with human hepatocytes, it is desirable to utilize a promoter that is not particularly active prenatally. Otherwise, such transgenic animals may die in utero. Other promoters inducible by agents that could be locally administered into the liver may also be suitable, such as the metallothionein promoter (which is inducible by heavy metal ions; Palmiter et al., 1982, Cell 29:701). Such genes are not specifically toxic to human hepatocytes, although there may be some "bystander effect" whereby a limited number of the human hepatocytes are killed." (Col. 13, lines 8-18). Wu et al. further state: "It may be preferable to effect stepwise attenuation of host hepatocytes rather than eliminate a majority in a short period of time, as the sudden loss of liver function could result in death of the animal and/or conditions that would disfavor the establishment of a human hepatocyte population in the host liver. For example, administration of several doses of gancyclovir to a host animal transgenic for the albumin promoter/HSV-TK construct, beginning before and continuing after introduction of donor cells, may result in a gradual elimination of host cells, thereby permitting human hepatocytes to establish a "foothold" before the majority of host hepatocyte function is eliminated." (col. 18, lines 52-63).

Thus, it is clear from that the teachings of Wu et al. comprise destroying some, but not all fetal liver tissue to avoid fetal death and allow the establishment of the transplanted tissue. Such is commensurate with the teachings of instant claim 1, that requires selective destroying of native cells in fetal liver and implanting foreign replacement cells.

Therefore the rejection of claims 1, 2, 5, 7 and 8 is maintained and further applied to new claims 13-21 for reasons of record and the foregoing discussion.

Response & New Claim Rejections - 35 USC § 103

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 1 and 3 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Wu et al. (U.S. Patent No.: 6,995,299; filed Aug. 15, 2001), in view of Loeb et al. (U.S. Patent No: 6,451,571; filed Sep. 17, 2002). The rejection set forth on pp. 3-4 of the office action dated

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August 20, 2007, and pp. 3-5 of the previous office action dated April 1, 2008 is maintained for claims 1, and 3, and further applied to new claim 22 for reasons of record.

Claims 1 and 9-12 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. (U.S. Patent No.: 6,995,299; filed Aug. 15, 2001), in view of Sorscher et al. (U.S. Patent No.: 6,017,896; filed Jun. 24, 1997). The rejections set forth on pp. 4-7 of the office action dated August 20, 2007, and pp. 3-5 of the previous office action dated April 1, 2008 is maintained for reasons of record.

Applicants traverse both rejections, arguing that Wu does not teach implanting foreign replacement cells in the fetus, or introducing hepatocytes prenatally. Applicants' arguments have been fully considered, but are not found persuasive.

Applicants are directed to the response provided above. Wu et al. describe propagation of human hepatocytes in non-human animals, wherein said animals have chimeric livers, whereby some of substantially all of the hepatocytes present are human hepatocytes (Title and Abstract), and wherein the animal comprising human hepatocytes is preferably a fetus (column 5, line 5). Further, as stated in MPEP 2123, "[t]he prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed..." *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

Therefore the rejection of claims 1, 3 and 9-12 are maintained and further applied to claim 22 for reasons of record and the foregoing discussion.

Conclusion

Claims 1-3, 5 and 7-22 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Examiner, Art Unit 1633